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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/816,708 | 04/02/2004 | Wendy Lea Corbett | 20892 US2 | 1192 |
| 151 | 7590 | 04/14/2008 | | EXAMINER |
| HOFFMANN-LA ROCHE INC. PATENT LAW DEPARTMENT 340 KINGSLAND STREET NUTLEY, NJ 07110 | | | KIM, ALEXANDER D | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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|------------------------------|--------------------------------------|---------------------------------------|
| Office Action Summary | Application No. 10/816,708 | Applicant(s) CORBETT ET AL. |
| | Examiner ALEXANDER D. KIM | Art Unit 1656 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 22 January 2008.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,3 and 4 is/are rejected.
- 7) Claim(s) 2 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/DS/02) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 08/21/2007), Applicants filed a response and amendment received on 01/22/2008. Said amendment amended Claims 1-4.

Claims 1-4 are pending in the instant Office action and will be examined herein.

Withdrawn-Compliance with Sequence Rules

2. The previous non compliance with the Sequence Rules is withdrawn by virtue of applicants' amendment.

Withdrawn-Objections to the Specification

3. The previous objection to the specification for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)) is withdrawn by virtue of Applicants' amendment.

Claim Objections

4. Claims 1-4 are objected to because of the following informalities: Claims 1-4 recites "Seq ID NO:1". It should be "SEQ ID NO: 1". Appropriate correction is required.

Withdrawn-Claim Rejections - 35 USC § 112

5. The previous rejection of Claims 1-3 under 35 U.S.C. 112, second paragraph, is withdrawn by virtue of Applicants' amendment.

6. The previous rejection of Claim 2 is rejected under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants' amendment.

7. The previous rejection of Claims 2 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' amendment.

Claim Rejections - 35 USC § 112

8. Claim 1 is rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 1-2. In response to this rejection, applicants have amended Claims 1-4 and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue the amendments in claim 1 reflecting the specific SEQ ID NO: 1 and deleting the term "about" for claimed co-crystal should place the claim into a condition for allowance.

Examiner acknowledge the amendment meets all requirements but one, i.e., the instant co-crystal still encompasses any ligand with unlimited structural limitations, which does not satisfy the written description requirement. As noted in the previous non final rejection, "for a species of crystal to be adequately structurally described, the following must be adequately disclosed: (1) the composition of the crystal [exact structural features of all molecules in the crystal must be described, including the protein (preferably a SEQ ID NO of all included residues) and any molecule bound to it], (2) the space group, and (3) the unit cell dimensions of the crystal." (emphasis added, see page 7, bottom). While the claim language requires a function for the instant genera of crystals (that of human glucokinase), the claims do not require, and the specification does not describe, any common characteristics that define the structure of the instant genera as a whole. One of skill in the art would be unable to predict the structure of other members of the genera by virtue of the disclosed species of the instant disclosure. While the structure and function of one species of said genera of mammalian glucokinase are disclosed in the specification, the common structural characteristics of species that define said genera are not described. Claims drawn to the instant genera of crystals are also not adequately described. Therefore, one skilled in the relevant art would be unable to make and use the claimed invention by virtue of the instant disclosure from the specification.

9. Claims 1 and 3-4 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a method for preparing

protein co-crystals of a polypeptide consisting of SEQ ID NO: 1 (GST-GK fusion protein) with ligands disclosed in Examples 3-10 that results in a crystal having the space group P6(5)22 and the unit cell dimensions within the range recited in Claims 1, does not reasonably provide enablement for all crystals and methods of preparation thereof as broadly encompassed by the claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous Claims 1-2. In response to this rejection, applicants have amended Claims 1-4 and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue amended Claims 1 and 3-4 (i.e., deleting the term "about" and adding the SEQ ID NO: 1) and 8 examples of ligands in the specification would clearly give guidance to one of ordinary skill in the art to make and use the other species of ligands. Thus, Applicants argue the instant claims meet all Wands factors and placed into a condition for allowance.

However, as previously noted, the breadth of the amended claims do not enable one skilled in the art to make and use the full scope of claims. Claims 1 are so broad as to encompass any co-crystal of SEQ ID NO: 1 with any ligand(s) having unlimited structural limitation. Claims 3 and 4 are drawn to a process for co-crystallization of SEQ ID NO: 1 in the presence of any allosteric ligand in a widely varying reservoir solution

recited in Claim 3. As previously noted, "the ability to crystallize a given protein was, at the least, challenging to a skilled artisan as even minor alterations in the conditions of crystallization could result in altered crystal forms, crystals of sub-diffraction quality, or a lack of crystal growth". One cannot predict *a priori* those conditions that will lead to the successful crystallization of a diffraction-quality crystal as evidenced by Kierzek et al. (2001, *Biophys Chem* 91:1-20), which teaches that "each protein crystallizes under a unique set of conditions that cannot be predicted from easily measurable physico-chemical properties" and that "crystallization conditions must be empirically established for each protein to be crystallized" (p. 2, left column, top). In view of these teachings, a skilled artisan would recognize that it is highly unpredictable as to whether diffraction-quality crystals of SEQ ID NO: 1 with any ligand. Thus, the disclosure of co-crystal with 8 ligands are not enough to overturn the unpredictability of crystallization that is generally known in the art at the time of instant filing date. Thus, applicant has not provided sufficient guidance to enable one skilled in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, preparation of any co-crystal encompassed in Claim 1 and crystallization methods in Claims 3-4 with desired characteristics of unit cell dimensions and space group is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Withdrawn-Claim Rejections - 35 USC § 102

9. The previous rejection of Claims 3 and 4 under 35 U.S.C. 102(b) as being anticipated by Aleshin et al. (2000, Mar. 3, J. Mol. Biol., volume 296, pages 1001-1015) is withdrawn by virtue of Applicants' amendment.

Conclusion

10. Claims 1-4 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652